June 12, 2002

Richard Henrich
Manager, Regulatory Affairs
Great Lakes Chemical Corporation
Highway 52 N.W.
West Lafayette, IN 47996

Dear Mr. Henrich:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Carbonic Acid, Oxydiethylene Diallyl Ester, posted on the ChemRTK HPV Challenge Program Web site on January 15, 2002. I commend Great Lakes Chemical Corporation. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Great Lakes Chemical Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK Challenge Submission:
Carbonic acid, oxydiethylene diallyl ester

Summary of EPA Comments

The sponsor, Great Lakes Chemical Corporation, submitted a Test Plan and Robust Study Summaries to EPA on December 20, 2001. EPA posted the cover letter, Test Plan and Robust Study Summaries on the Chem RTK Web site on January 15, 2002. The proposed information gathering plan is for Carbonic acid, oxydiethylene diallyl ester (CAS No. 142-22-3).

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. The submitter needs to provide measured vapor pressure and water solubility data.

2. Health Effects. EPA agrees with the submitter that data need to be generated to address repeated-dose toxicity, reproduction toxicity and chromosomal aberration endpoints. However, EPA disagrees with the submitter's proposal to conduct an assessment of toxicity to reproductive organs in its proposed 90-day repeated-dose toxicity study to address the reproductive toxicity endpoint. EPA recommends conducting a Combined Repeated-dose Toxicity Study with the Reproduction/Developmental Toxicity Screen (OECD 422).

1. Ecotoxicity: Algae. (a) The submitter needs to explain use of a solvent in the algal toxicity studies. (b) The submitter needs to provide an EC_{50} value based on number of cells/mL. If an adequate explanation for using the solvent is not provided and an algal EC_{50} value cannot be calculated, the submitter needs to conduct an algal toxicity test without the use of a solvent.

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.

EPA Comments on the Carbonic Acid, Oxydiethylene Diallyl Ester Challenge Submission

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

Adequate data are available for melting point, boiling point, and partition coefficient for the purposes of the HPV Challenge Program.

The submitter needs to provide measured vapor pressure data because the estimated value of ca. 1.46×10^{-4} kPa at 25 °C is higher than 10^{-5} kPa, the SIDS threshold for vapor pressure testing.

The submitter provided a water solubility value of < 0.1 g/l at 20 °C. Qualitative values are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide a discrete measured water solubility value for this chemical.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Adequate data are available for photodegradation, biodegradation, and fugacity for the purposes of the HPV Challenge Program.

EPA agrees that a stability in water test is necessary.

Health Effects (acute, repeated-dose, genetic, and reproductive/developmental toxicity).

EPA agrees with the submitter that data need to be generated to address repeated-dose toxicity, reproduction toxicity and chromosomal aberration endpoints. EPA recommends conducting a Combined Repeated-dose Toxicity Study with the Reproduction/Developmental Toxicity Screen (OECD 422).

Acute Toxicity. Although there are deficiencies in the data analyses, the overall weight of evidence indicates that this endpoint has been adequately addressed for the purposes of the HPV Challenge Program.

Repeated-dose toxicity. The two 14-day dermal toxicity studies are not of sufficient duration and appropriate route of exposure to adequately characterize the repeated-dose toxicity of this compound. EPA recommends conducting a Combined Repeated-dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422) to address this endpoint.

Reproductive toxicity. EPA disagrees with the submitter's plan to evaluate toxicity to reproductive organs in the proposed 90-day repeated-dose study. This approach is not adequate for the purposes of the HPV Challenge Program. EPA's HPV Challenge Guidance specifies that such an assessment of toxicity to reproductive organs is acceptable only in the case of an existing 90-day study when an acceptable developmental toxicity study is available. EPA recommends that the submitter conduct a Combined Repeated-dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422) to address this endpoint.

Ecotoxicity (fish, invertebrates, algae)

EPA agrees with the submitter that the endpoints for acute toxicity to fish and invertebrates have been adequately addressed; however, the submitter needs to address several deficiencies in the robust summaries.

Algae. For the algal toxicity testing, triethylene glycol was used as a solvent. The submitter needs to provide an explanation for using a solvent in the algal study. The submitter also needs to provide an EC_{50} value based on the cell count (number of cell/mL). If this issue is not adequately addressed, the submitter needs to conduct a new study according to the OECD guideline 201.

Specific Comments on Robust Summaries

General. All robust summaries indicate that the test substance was as prescribed by 1.1 - 1.4. However, the submitter did not provide purity of the test substance in these sections and needs address this issue.

Health Effects:

Acute toxicity. The submitter needs to recalculate the LD_{50} derivations in the key acute oral toxicity study (Ref. 6), particularly for male rats, as the reported LD_{50} is not consistent with the experimental data.

Genotoxicity (gene mutations). The results of the single assay gave positive (ambiguous) results for one of five test strains of *Salmonella.* It is likely that the positive response was a consequence of an unusually low response in the solvent controls. Therefore, the original test data needsto be re-examined to confirm that the test chemical is nonmutagenic as claimed by the submitter. If the submitter plans to

conduct a new assay, it would be better if the test material were purified further.

Developmental Toxicity. The submitter needs to include a maternal NOAEL, the magnitude of the body weight losses and the number of litters available for examination.

Ecotoxicity (fish, invertebrates, algae)

The acute toxicity endpoints for daphnia and fish were missing percent purity, pH, and DO in some of the robust summaries.

Follow-up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.